

1. An apparatus for deposit of fluid samples in an array of mutually isolated dots, comprising a deposit device, a fluid source for repeatedly providing a discrete drop of fluid on the deposit device, mechanism for moving  
5 the device relatively over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving the device, relatively, toward and away from the receiving substrate to deposit respective drops of fluid at respective deposit locations on the substrate by direct  
10 contact of drops of fluid on the deposit device with the substrate without direct contact of the deposit device with the substrate.

2. The apparatus of claim 1 in which the deposit device is flexibly mounted and associated with a dampener  
15 that enables compliant, dampened contact of the device with the substrate via an intervening film of the fluid.

3. The apparatus of claim 1 or 2 wherein the deposit device is a moveable pin.

4. The apparatus of claim 1 wherein the fluid  
20 source includes a fluid storage device relative to which the deposit device repeatedly moves to resupply the device during the deposit of successive drops.

5. The apparatus of claim 4 in which the fluid storage device is a local fluid storage device generally  
25 movable over the array of deposit locations, the fluid storage device being constructed and arranged to resupply the deposit device at various locations with respect to the array.

6. The apparatus of claim 5 in which the local fluid storage device and the deposit device are coupled for transverse motion across the array.

5 7. The apparatus of claim 6 in which the local fluid storage device and the deposit device are decoupled for movement toward and away from the substrate.

8. The apparatus of claim 5 in which the local storage device is constructed and arranged to be replenished from a remotely located relatively large reservoir.

10 9. The apparatus of claim 8 in which the reservoir is constructed to store a multiplicity of isolated fluid volumes, the apparatus constructed to move the local supply device to a selected fluid volume of said reservoir for replenishment.

15 10. The apparatus of claim 9 in which the volumes comprise the wells of a plate and the local storage device is constructed to dip into the well.

20 11. The apparatus of claim 10 in which the local storage device has a fluid retaining surface having a surface roughness of at least 1000 microinch.

12. The apparatus of claim 5 constructed to produce relative resupply movement between the deposit device and the local storage device for the deposit of each discrete fluid drop.

25 13. The apparatus of claim 5 in which the deposit device is a moveable pin and the local storage device

includes a member which defines a generally annular fluid retention surface, and the deposit pin is constructed to move within the annular retention surface from retracted to extended positions, in the retracted position the deposit  
5 end of the pin being retracted from the lower surface of fluid retained by the annular surface of the storage device, and in the extended position the deposit end of the pin being projected beyond the lower surface of the retained fluid.

10 14. The apparatus of claim 13 in which the annular surface is generally aligned with the pin and a driver is associated with the member that defines the annular surface to move the member generally linearly downwardly beyond a position of a deposit end of the pin to a replenishment  
15 position, the pin and the member defining the annular surface and associated drivers being movable to the cleaning system, and to a replenishment region in which the annular member is replenished.

20 15. The apparatus of claim 1 in which the deposit device is mounted on a flexure which constrains the device to a predetermined path of travel, and a driver is engaged to cause reciprocal motion constrained by the flexure, between retracted and extended positions depending upon the position of the driver.

25 16. The apparatus of claim 1 in which a stable spring is arranged to urge the deposit device in the direction opposite to the deposit motion.

17. The apparatus of claim 1 in which the deposit device is constrained in its path of motion by at least one planar flexure.

18. The apparatus of claim 1 in which the deposit  
5 device is mounted on a pair of parallel flexures that maintain the deposit device at a constant angle to a surface on which the drops are deposited.

19. The apparatus of claim 18 in which the parallel flexures are cantilevered and the deposit device is on the  
10 free end of the assembly.

20. The apparatus of claim 19 in which at least one of the flexures includes a metal spring element.

21. The apparatus of claim 19 in which at least one of the flexures includes a damping element.

15 22. The apparatus of claim 21 in which the damping element is a damping layer laminated to a spring layer.

23. The apparatus of claim 22 comprising a lamination of a metal spring layer and a damping layer.

24. The apparatus of claim 22 in which the flexure  
20 includes a spring layer laminated on opposite sides of a damping layer.

25. The apparatus of claim 1 in which the deposit device is mounted on a multiple flexure system.

26. The apparatus of claim 25 in which at least one relatively stiff flexure supports the deposit device via at least one intermediate relatively compliant flexure, a driver engaged, effectively, with the relatively stiff flexure, and the deposit device being free to deflect by action of the compliant flexure, upon encountering resistance when moving toward the substrate.

27. The apparatus of claim 1 in which the deposit device is arranged to engage the substrate via a film of the fluid with a pressure less than about 1 gram.

28. The apparatus of claim 1 in which the deposit device has a natural frequency of at least 10 Hz.

29. The apparatus of claim 1 including a cleaning system, and a control system adapted to control relative movement of the deposit device to a depositing relationship to the substrate and a cleaning relationship to the cleaning system.

30. The apparatus of claim 29 in which the deposit device is associated with a local supply device that travels with it, the deposit device and local supply device movable together to the cleaning system.

31. An apparatus for deposit of fluid samples in a dense array of mutually isolated dots, comprising a deposit device, a fluid source for repeatedly providing fluid to the deposit device, mechanism for moving the device relatively over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving the deposit device, relatively, toward and away from the

receiving substrate to deposit respective drops of fluid at respective deposit locations on the substrate, and a control system adapted to control relative movement of the deposit device to a deposit relationship with the substrate, wherein  
5 the deposit device is mounted on a flexure system which constrains the device to precise motion, and a driver is engaged to drive the deposit device to enable reciprocal motion, constrained by the flexure system, between retracted and extended positions depending upon the position of the  
10 driver.

32. The apparatus of claim 31 in which the flexure system is constructed to maintain substantially a constant angle between the deposit device and the substrate as the deposit device approaches the substrate.

15 33. The apparatus of claim 32 in which the flexure system comprises a pair of parallel flexures.

34. The apparatus of claim 33 in which the flexures are comprised of a leaf spring.

20 35. The apparatus of claim 32 in which the flexure system comprises a single flexure.

36. The apparatus of claim 32 in which the deposit device is mounted on a multiple flexure system.

37. The apparatus of claim 35 in which a relatively stiff flexure supports the deposit device via an  
25 intermediate relatively compliant flexure, the driver for the device engaged, effectively, with the relatively stiff flexure, and the deposit device being free to deflect

relative to the stiff flexure by action of the compliant flexure, upon encountering resistance when moving toward the substrate.

38. An apparatus for deposit of fluid samples in a  
5 dense array of mutually isolated dots, comprising a deposit pin, a fluid source for repeatedly providing a drop of fluid on the end of the deposit pin, mechanism for moving the pin relatively over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving  
10 the pin, relatively, toward and away from the receiving substrate to deposit respective drops at respective deposit locations on the substrate, and wherein the pin is mounted on a flexure system which constrains the pin to a predetermined path of travel, and a driver is engaged to  
15 drive the pin to enable reciprocal motion, constrained by the flexure system, between retracted and extended positions depending upon the position of the driver.

39. An apparatus for deposit of fluid samples in a dense array of mutually isolated dots, comprising at least  
20 two deposit pins, at least one fluid source for repeatedly providing a drop of fluid on the end of each deposit pin, mechanism for moving the pins together transversely over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving each pin  
25 independently, relatively, toward and away from the receiving substrate to deposit respective drops at respective deposit locations on the substrate.

40. The apparatus of claim 39 constructed to mount a number of microscope slides to serve as said substrate in  
30 deposit-receiving relationship, and a control system

constructed and arranged to move the deposit pins in the manner to form deposits on more than one slide.

41. The apparatus of claim 39 in which at least four such pins and drivers are mounted on a deposit head.

5           42. A deposit mechanism for deposit of biological fluid dots in an array, comprising a pin supported by a flexure, a source of biological fluid for deposit, and a driver engaged to drive the pin to enable reciprocal motion constrained, between retracted and extended positions  
10 depending upon the position of the driver.

43. The apparatus of claim 42 including a discrete local fluid supply for the pin.

          44. The apparatus of claim 43 in which a member defines a generally annular fluid retention surface, and the  
15 deposit pin is constructed to move within the annular retention surface from retracted to extended positions, in the retracted position the deposit end of the pin being retracted from the lower surface of fluid retained by the annular surface of the storage device, and in the extended  
20 position the deposit end of the pin being projected beyond the lower surface of the retained fluid.

          45. The apparatus of claim 44 in which a driver is arranged to move the annular member generally downwardly beyond the deposit end of the pin to a replenishment  
25 position.

46. The apparatus of claim 45 in which the flexure-mounted pin and the member defining an annular retention surface are associated with respective drivers.

47. The apparatus of claim 45 in which the pin and member are movable as an assembly to a station for cleaning, and to a replenishment region in which the member is replenished from a selected source.

48. The apparatus in which at least four pin and annular member assemblies according to claim 45 are clustered for movement together transversely over the substrate.

49. The apparatus in which two or more deposit pins according to claim 44 are grouped together for movement by a single drive and a corresponding number of members defining annular fluid retention surfaces according to claim 44 are associated respectively with respective pins, the members driven by a single drive member.

50. An apparatus for deposit of fluid samples in a dense array of mutually isolated dots, comprising a deposit device, a source of fluid for the deposit device, mechanism for moving the deposit device relatively over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving the deposit device, relatively toward and away from the receiving substrate to deposit respective drops of fluid at respective deposit locations on the substrate, a cleaning system, and a control system adapted to control relative movement of the deposit device between a resupply relationship to the source, a

depositing relationship to the substrate and a cleaning relationship to the cleaning system.

51. The apparatus of claim 50 wherein the source includes a fluid storage device relative to which the deposit device repeatedly moves to resupply the device during the deposit of the isolated drops of fluid.

52. The apparatus of claim 51 in which the fluid storage device is a mobile local fluid storage device generally movable with the deposit device over the array of deposit locations, the fluid storage device being constructed and arranged to locally resupply the deposit device during its deposit sequence.

53. The apparatus of claim 52 in which the local storage device is constructed and arranged to be replenished from a remotely located relatively large reservoir.

54. The apparatus of claim 53 in which the reservoir is constructed to store a multiplicity of isolated fluid volumes, the apparatus constructed to move the local supply device to a selected fluid volume of said reservoir for replenishment.

55. The apparatus of claim 53 constructed to produce relative resupply movement between the deposit device and the local storage device for the deposit of each discrete drop.

56. The apparatus of claim 52 in which the local supply device is driven to enter a supply well and having a

surface adapted to retain a supply of fluid by surface tension or capillary effects.

57. The apparatus of claim 40 in which a retaining surface of the local supply has surface roughness of at  
5 least 1000 microinch.

58. The apparatus of claim 41 in which a member has an inner annular surface having the surface roughness.

59. The apparatus of claim 44 in which the member has an outer surface that is generally cylindrical.

10 60. The apparatus of claim 44 sized and constructed to enter a well of a PCR plate and extract fluid by surface position or capillary efforts for supply to the deposit device.

61. Apparatus for automated preparation of a  
15 microscope slide, comprising a microscope slide holder, a carrier operative over a slide on the holder, and a deposition head mounted on the carrier, the deposition head including a deposit pin constructed to carry a drop of fluid from a fluid supply, and mechanism constructed, in a deposit  
20 sequence, to move the deposit pin relative to the supply to pick up a drop of fluid, and move the deposit pin toward the microscope slide to completely deposit the drop of fluid on the slide, there being a control system arranged to repeat the deposit sequence to produce a high density of drops of  
25 deposited fluid upon the slide.

62. The device of claim 61 in which the deposit pin has a deposit end comprising an abrupt profile that defines the perimeter of the drop of fluid to be picked up.

63. The device of claim 62 in which the pin  
5 comprises a generally cylindrical shaft and an end rim.

64. The deposition head of claim 63 in which the end rim is defined by a generally planar butt end of the pin.

65. The device of claim 61 wherein the supply  
10 comprises a sub-reservoir mounted on the head, closely adjacent to the deposit pin.

66. The device of claim 61 or 65 constructed to prepare a series of slides in identical manner, the carrier constructed to hold a series of slides, and the control  
15 system constructed to deposit a drop of a given composition upon identical locations on the series of slides, by respective movements of the head.

67. The device of claim 66 in which the deposition head comprises a multiplicity of said deposit pins ganged to  
20 form a multiplicity of drops.

68. The device of claim 66 in which the deposit pins are associated with respective discrete drivers.

69. The device of claim 67 in which the deposit pins are associated with a single driver.

70. The device of claim 61 wherein the deposition head comprises an annular supply ring constructed to be immersed in and withdrawn from a well of a sample-containing reservoir to retain between wall portions of the annular ring a supply of fluid carrying material to be examined, the deposit pin being operative within the annular ring to move generally axially between a retracted position in which a deposit end of the pin is withdrawn above an exposed surface of the retained sample, and an extended position in which a dot of the fluid is carried on the end of the pin for deposit on the slide.

71. The device of claim 61 or 70 in which the deposit pin is mounted on at least one flexure that constrains the deposit pin to a predetermined path of travel relative to the head.

72. Apparatus for deposit of fluid samples in a dense array of mutually isolated dots on a receiving surface comprising a deposit pin, a fluid source for repeatedly providing a drop of fluid on the end of the deposit pin, mechanism for moving the pin relatively over an array of spaced apart deposit locations of a receiving substrate, mechanism for repeatedly moving the pin, relatively, toward and away from a targeted point on the receiving substrate to deposit respective drops of fluid at respective deposit locations on the receiving surface, and means for stopping movement of the depositing pin toward the targeted point on the receiving surface while fluid remains between the end of the pin and the receiving surface.

73. The apparatus of claim 72 in which said means comprises a compliant system that limits the motion of the pin in response to resistance force transmitted to the pin.

5 74. The apparatus of claim 73 in which the resistance force is predetermined to be less than the total displacing force required to cause the pin to displace the fluid so much that the pin makes solid contact with the receiving surface.

10 75. The apparatus of claim 74 in which a spring system mounting the deposit pin limits the force with which the deposit pin presses toward the receiving surface.

76. The apparatus of claim 75 in which the deposit pin is coupled to the driver by a weak spring of selected spring value.

15 77. The apparatus of claim 76 in which the strength of the spring is selected to enable the deposit pin to cease movement toward the receiving surface before termination of movement of the driver.

20 78. The apparatus of claim 70 or 61 in which over-travel of the driver of the pin toward the receiving surface is permitted by the weak spring without significant effect upon the spacing of the end of the pin from the receiving surface.

25 79. The apparatus of claim 73 in which the compliant system including a leaf spring or flexure.

80. The apparatus of claim 76 in which the weak spring is supported on a relatively stiff spring engaged by the driver for moving the deposit pin.

81. An apparatus comprising a deposit pin  
5 constructed and arranged to deposit a first dot upon a substrate and thereafter, in registration, to deposit a second dot upon the first dot.

82. The apparatus of claim 81 in combination with a source of multiple fluids comprising a first fluid for said  
10 first dot and a second fluid for the second dot, the first and second fluids selected to potentially interact.

83. The apparatus of claim 81 including a device for depositing a large spot of a given reagent and a device for depositing dots of smaller size of different reagents  
15 upon the deposited large dot.

84. A fluid deposit arrayer for transferring a drop of fluid to a substrate by engaging the drop with the substrate, the device mounted on a compliant spring for compliant engagement with the substrate and incorporating a  
20 motion damping member.

85. The fluid deposit arrayer of claim 84 in which the spring comprises a flexure mounting.

86. The arrayer of claim 85 in which at least one portion of the flexure mounting comprises a composite in  
25 which a layer of flexible damping material is bonded to a flexure member.

87. The arrayer of claim 86 in which a pair of flexure members are bonded together in a composite sandwich containing a layer of damping material.

88. The arrayer of claim 86 in which the flexible  
5 damping layer comprises a rubber or rubber-like compound.

89. The arrayer according to claim 87 in which at least one of the flexure layers of the composite is a resilient plastic layer.

90. The arrayer according to claim 89 in which at  
10 least one of the flexure layers comprise polyamide.

91. The arrayer according to claim 87 in which one of the flexure layers comprises a spring metal and the other layer comprises a bonding material having damping characteristics.

92. The arrayer according claim 85 in which the  
15 flexure is a planar flexure about 8mm in width and between about 20 and 25mm in length.

93. The arrayer according to Claim 87 in which a layer of flexible resin is laminated by rubber cement to a  
20 flexible metal layer.

94. The arrayer of claim 84 in which a deposit pin is mounted upon a pair of parallel flexures.

95. The arrayer of claim 94 in which at least one of the flexures comprises spring metal, and the other

comprises, at least in part, a material having greater dampening properties than said spring metal.

96. The arrayer of Claim 94 in which each parallel flexures comprise a lamination according to claim 93.

5           97. The arrayer of claim 84 having a natural frequency greater than about 10HZ.

98. A deposit head including at least two flexure mounted pins, and a single actuator arranged to move the pins simultaneously from supply to deposit positions, the  
10 head mounted for lateral movement in both X and Y axes.

99. The deposit head of 98 in which the pins are spaced apart 9mm.

100. A deposit head including at least two flexure mounted pins, each associated with its own actuator to be  
15 moved independently from supply to deposit position, the head mounted for lateral movement in both X and Y axes.

101. The deposit head of claim 100 in which the pins are spaced apart 9 mm.

102. An aliquot carrier defining a fluid-retaining  
20 aperture through which a deposit device can transit to pick up a drop of fluid to be deposited, internal surfaces defining said aperture having a surface roughness that increases its wettability.

103. The carrier of claim 102 in which the surface  
25 roughness is produced by a technique selected from the class

of sanding, broaching, machining, screw or knurl forming, coating or forming the surface of particles that provide surface roughness as by sintering or molding.

104. The carrier of claim 102 in which the surface  
5 roughness is at least 100 microinch.

105. A process of printing comprising, under computer control, moving at least one flexure mounted pin to selected X,Y positions, and depositing with said pin, a desired material.

106. The method of claim 105 in which the material  
10 is an ink or dye.

107. The method of claim 106 in which the material is a photoresist material.

108. The method of claim 105 in which the material  
15 is a varnish or encapsulant.

109. A method of causing a biological compound to interact with another substance at a predetermined position on a substrate the step comprising depositing at least one of the compound or reagent in a precisely determined  
20 localized spot relative to the substrate by mechanically lowering a compliant pin, to which a drop of the compound or reagent is adhered by surface tension, toward the substrate until the drop contacts the substrate or a pre-applied compound on the substrate with the pin executing a  
25 controlled force of less than a gram thereon, and thereafter mechanically lifting the pin away from the substrate under

conditions in which the fluid drop transfers to the substrate or the pre-applied compound on the substrate.

110. The method of claim 109 in which drops of both the compound and the other substance are successively  
5 deposited by the technique of claim 92.

111. The method of claim 109 in which the pin, when approaching the substrate, applies a force to the substrate with a force of about 0.5 grams.

112. The method of claim 109 in which the compliant  
10 pin is mounted upon a support by flexures that constrain the pin to substantially linear motion relative to the support, and moving the support carrying the flexures and pin toward the substrate in an overtraveling linear motion parallel to the direction to which the pin is constrained to deflect,  
15 during which motion the pin engages the substrate or pre-applied compound on the substrate, and the flexures deflect in response to resistance encountered by the pin, thereby cushioning the contact of the pin.

113. The method of claim 109 in which a supply of  
20 the biological compound or substance to be deposited by the pin is supported above the substrate at the deposit location within a ring by surface tension, and the pin is lowered through the ring in the manner that a relatively small drop of the reagent from the supply is adhered to the end of the  
25 pin by surface tension.

114. The method of claim 109 in which the fluid to be deposited from fluid selected the group of fluids described in the specification.

115. The method of depositing a biological fluid  
with a pin comprising supporting fluid within a ring by  
surface tension, and the pin is lowered through the ring in  
the manner that a relatively small drop of the reagent from  
5 the supply is adhered to the end of the pin by surface  
tension.